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| 10/705,615 | 11/10/2003 | Xiaobo Wang | ACE-00101.P.1.2-US | 4696 |

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| EXAMINER | |
|---|---|
| BEISNER, WILLIAM H | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/705,615 | WANG ET AL. | |
| | Examiner | Art Unit | |
| | William H. Beisner | 1744 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 June 2007 and 09 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2,6,9-11,24,25,28,29,36,43,50,51,62,65,68,69 and 138-153* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,9-11,24,25,28,29,36,43,50,51,62,65,68,69,138-145,147 and 151-153* is/are rejected.

7)☒ Claim(s) *146 and 148-150* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/9/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Information Disclosure Statement*

1. The information disclosure statement filed 7/9/2007 has been considered and made of record.

### *Claim Objections*

2. Claims 146 and 148-150 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits. Note claims 146 and 148 recite they depend from two separate claims and have not used alternative language.

### *Claim Rejections - 35 USC § 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 6, 8-11, 24, 25, 28, 29, 49, 138, 143-145, 147 and 151-153 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Picard (US 2004/0091397) or Tchao (US 5,601,997) in view of Lynes et al.(US 6,723,523).

Both of the references of Picard and Tchao disclose devices for monitoring the migration or invasion of biological particles.

The reference of Picard discloses an upper chamber (114); a lower chamber (116); a biocompatible porous membrane (106) having a porosity sufficient to allow cells to migrate there through and the membrane (106) separates the upper and lower chambers (See Fig. 1B).

The reference of Tchao discloses an upper chamber (24); a lower chamber (22,28); a biocompatible porous membrane (10) having a porosity sufficient to allow cells to migrate there through and the membrane (10) separates the upper and lower chambers (See Fig. 2).

With respect to claim 1, while both of the references of Picard and Tchao disclose the use of optical detection devices (See sensor 120 of Picard and detector 30 of Tchao) for detecting the

presence of cells within the lower chamber, the references do not disclose that at least two electrodes are present in the lower chamber for detecting the presence of cells by a change in impedance between the electrodes.

The reference of Lynes et al. discloses that it is known in the art to employ impedance sensing electrodes within a cell or culture space for detecting the presence and/or movement of a cell in response to a chemotactic gradient (See column 9, lines 55-67).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to replace the optical detection systems of the primary references with an impedance measurement system suggested by the reference of Lynes et al. for the known and expected result of providing an alternative means recognized in the art to detect or sense the presence of cells within the lower chambers of the test devices. The reference of Lynes et al. discloses advantages such as improved quantitation of the number of cells (See column 2, lines 58-65).

With respect to claim 2, all of the references disclose that the detection or sensing is performed at the bottom of the chamber.

With respect to claim 6, the reference of Lynes et al. discloses the use of impedance analyzer (60).

With respect to claims 8 and 25, the references of Picard and Tchao disclose that the membranes can be made of a polymer material (See paragraph [0029] of Picard and column 6, lines 10-45, of Tchao). Furthermore wiith respect to claim 8, while the references are silent with respect to the thickness of the membrane, if not inherently met, it would have been obvious to one of ordinary skill in the art to determine the optimum thickness while maintaining the structural integrity of the membrane and efficiency of the detection system.

With respect to claims 9, 24, 28 and 29, based on the specifics of the assay to be performed, it would have been obvious to one of ordinary skill in the art to coat the membrane for cell attachment when required.

With respect to claim 10, the reference of Lynes et al. discloses the use of conductive traces and connection devices (See Figure 2).

With respect to claim 11, both the systems of the modified primary references would meet the limitations of claim 11 since both devices are intended to be used for determination of cells moving into the lower chambers.

With respect to claim 49, the reference of Lynes et al. discloses that an array of electrodes can be employed to detect the presence of cells (See Figure 2).

With respect to claims 24, 138 and 144, whether the electrodes are provided on the bottom of the chamber or the bottom of the membrane would have been well within the purview of one having ordinary skill in the art while maintaining the require electrodes for detecting the presence of cells within a chamber of the device.

With respect to claim 143, both the references of Picard and Tchao disclose the use of plates that include one or more wells (See Figure 10A and 10B of Picard and Figure 1 of Tchao).

With respect to claim 145, it would have been obvious to one of ordinary skill in the art to position the electrodes in any chamber of the device in which cells are intended to be used such that the presence of cells in a chamber can be monitored as is required of the device of the modified primary reference. With respect to the pore diameter, if the references of Picard and Tchao do not inherently meet the claimed pore size, it would have been obvious to one of

ordinary skill in the art to optimize the pore size based merely on the size of the cell to be used within the test device while maintaining the efficiency of the detection system.

With respect to claim 147, the membranes of the references of Picard and Tchao are capable of supporting epithelial or endothelial cells.

With respect to claims 151-153, both the systems of the modified primary references would meet the limitations of claims 151-153 since both devices are intended to be used for determination of cells moving into the lower chambers. If not, it would have been obvious to one of ordinary skill in the art to determine the optimal chamber in which to add chemicals based merely in the intended assay to be performed while maintaining the efficiency of the assay.

5. Claims 9, 24, 25, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Picard (US 2004/0091397) or Tchao (US 5,601,997) in view of Lynes et al.(US 6,723,523) taken further in view of Springer et al.(US 5,514,555).

The combination of the references of Picard or Tchao with Lynes et al. has been discussed above.

With respect to the use of a cell adhesion material within the membrane and/or the device, the reference of Springer et al. discloses that is it known to use a membrane coated with collagen (See column 10, lines 47-50).

With respect to the use of a layer of endothelial cells, the reference discloses using a coating of cells of one type on the membrane where a cell of another type passes through the membrane (See column 10, lines 27-67).

In view of this disclosure, it would have been obvious to one of ordinary skill in the art perform the assays disclosed by the reference of Springer et al. in the system of the modified primary reference for the known and expected result of providing an art recognized means for determining the passage of cells from one chamber into the other. As a result, the membrane would include cell adhesion material and include a porosity that prevents the passage of endothelial cells while allows the passage of lymphocytes. Whether the chemoattractant is provided in the upper chamber or lower chamber would have been within the skill on one having ordinary skill in the art while maintaining the function of the device.

With respect to the position of the electrodes, whether the electrodes are positioned on the bottom of the chamber or directly on the lower surface of the membrane would have been entirely within the purview of one having ordinary skill in the art based merely on the size of the chamber employed. One of ordinary skill in the art would recognize that the cell would be detected earlier if provided on the membrane rather than the bottom of the chamber.

6. Claims 36, 43, 50, 51, 62, 65, 68, 69 and 139-142 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Picard (US 2004/0091397) or Tchao (US 5,601,997) in view of Lynes et al.(US 6,723,523) taken further in view of Ehret et al.(Biosensors).

The combination of the references of Picard or Tchao with Lynes et al. has been discussed above.

Claims 36, 43, 50, 51 and 139 differ by reciting that the electrodes are of the same surface area and/or are interdigitized.

The reference of Ehret et al. discloses that it is known in the art when measuring cell behavior within a culture chamber to employ impedance detection electrodes that are of the same surface area and/or are interdigitized (See Fig. 1).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ an impedance detection system as disclosed by the reference of Ehret in the system of the modified primary reference for the known and expected result of providing an alternative means recognized in the art to achieve the same result, measuring cell behavior or presence on a surface by impedance analysis.

With respect to claims 50 and 51, when using multiple chambers as disclosed by the references of Picard and Tchao, multiple pairs of electrodes would be uniformly distributed between the separate test chambers.

With respect to claim 62, if the references of Picard and Tchao do not inherently meet the claimed pore size, it would have been obvious to one of ordinary skill in the art to optimize the pore size based merely on the size of the cell to be used within the test device while maintaining the efficiency of the detection system.

With respect to claim 65, if the references of Picard and Tchao do not inherently meet the claimed surface coating, it would have been obvious to one of ordinary skill in the art to optimize the surface properties of the membrane based merely on the type of the cell to be used or cultured within the test device while maintaining the efficiency of the detection system.

With respect to claims 68 and 69, both the systems of the modified primary references would meet the limitations of claims 68 and 69 since both devices are intended to be used for determination of cells moving into the lower chambers. If not, it would have been obvious to

one of ordinary skill in the art to determine the optimal chamber in which to add chemicals based merely in the intended assay to be performed while maintaining the efficiency of the assay.

With respect to the shape and dimensions of claims 140 and 141, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to optimize the design of the interdigitized electrodes based merely on the types of cells to be detected in the system while maintaining the efficiency of the detection system.

With respect to claim 142, the references of Lynes et al. and Ehret et al. disclose the use of impedance analyzers.

***Response to Arguments***

7. With respect to the rejection of Claims 1-11, 24, 25, 28, 29, 32 and 49 under 35 U.S.C. 103(a) as being unpatentable over either Picard (US 2004/0091397) or Tchao (US 5,601,997) in view of Lynes et al.(US 6,723,523), Applicants argue that the rejection is improper for a number of reasons as set forth below:

i) With respect to claims 1 and 24, the reference of Lynes employs an ECIS electrode system wherein the device requires a small sensing electrode and a large while the instant invention functions in a different manner. Applicants stress that all of the electrodes can be used to monitor impedance rather than just the sensing electrode of Lynes (See pages 19-20 and 22-23 of Applicants' response filed 6/21/2007.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., all the electrodes of the device can be used to monitor impedance) are not recited in the rejected

claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In this case, Applicants' comments are not commensurate in scope with the instant claim language.

ii) With respect to claims 1 and 24, the reference of Lynes requires a chemical gradient stabilizing medium which is not required of the instant invention or the references of Picard or Tchao (See pages 20-21 and 23-24 of Applicants' response filed 6/21/2007).

In response to applicant's argument that a chemical gradient stabilizing medium is required, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this case, one of ordinary skill in the art would clearly recognize that the electrode structure disclosed by the reference of Lynes is not limited to the preferred embodiment of the reference of Lynes. This is clearly evidence by the disclosure of Lynes at column 3, line 54, to column 4, line 37.

8. With respect to the rejection of Claims 9, 24, 25, 28, 29, 30, 32 and 60-69 under 35 U.S.C. 103(a) as being unpatentable over either Picard (US 2004/0091397) or Tchao (US 5,601,997) in view of Lynes et al.(US 6,723,523) taken further in view of Springer et al.(US 5,514,555) and the rejection of Claims 36, 43, 44, 50 and 51 under 35 U.S.C. 103(a) as being unpatentable over either Picard (US 2004/0091397) or Tchao (US 5,601,997) in view of Lynes et

al.(US 6,723,523) taken further in view of Ehret et al.(Biosensors), Applicants argue (See pages 25-26 of the response filed 6/21/2007) that the additional references cited in the rejection do not cure the deficiencies argued previously with respect to claims 1 and 24 over the combination of either Picard or Tchao in view of Lynes et al.

In response, the Examiner maintains that the combination of the references of Picard or Tchao with Lynes et al. is proper for the reasons already of record. The additional references of Springer et al. and Ehret et al. were relied upon to address the further claim limitations of the dependent claims.

***Conclusion***

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys J. Corcoran can be reached on 571-272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner
Art Unit 1744

WHB